REMARKS

Applicants submit these remarks in response to the Office Action mailed May 11, 2005. Claims 1 and 5-11 are pending. Applicants acknowledge that the rejection of claims 1 and 5-11 under 35 U.S.C. § 102(e), and of claim 1 under 35 U.S.C. § 102(b), have been withdrawn (Office Action, paragraph 4).

1-4. No response required.

5. Claims 1 and 5-11 are provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 1-11 of copending application No. 10/200,026. Applicants will file a terminal disclaimer at the appropriate stage when allowable subject matter is indicated in this application.

6. Claims 1 and 5-11 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Reconsideration and withdrawal of this rejection are respectfully requested. Applicants reiterate that the state of the art has progressed considerably since 1988, and that one of skill would be familiar with more advanced methods of protein chemistry at the time of the filing the application 12 years later. Claim 5 recites between one and ten conservative amino acid substitutions, as disclosed at page 14, lines 10-15 of the specification. As stated previously, the only changes disclosed in relation to "conservative" amino acid substitutions are those "preferably of a minor nature" that "do not significantly affect the folding or activity of the protein." (Page 14, lines 10-12.) This statement addresses the Examiner's concern (Office Action, pages 4-5) that the specification does not provide the standard used in assessing if these substitutions would significantly affect the folding or activity of the protein.

The Examiner also questions the enablement of implementing SEQ ID NO:2 in cancer diagnosis, stating, "the experimental design presented in the specification lacks information regarding the applicability of SEQ ID NO:2 and complements thereof in diagnostic methods relative to breast cancer." (Page 5, lines 9-11.) In fact, the specification has ample evidence of such enablement as discussed below.

Example 2 discloses the differential expression of SEQ ID NO:1, which encodes SEQ ID NO:2, in breast cancer cell lines. Expression of SEQ ID NO:1 was measured in the highly metastatic cell lines MDA-MB 231 and MDA-MB 435, and compared with low

metastatic or non-metastatic breast cancer cell lines. In all cases, there was increased expression of SEQ ID NO:1 in human breast cancer cell lines derived from human tumors with high metastatic potential. This diagnostic function is consistent with expression of the protein product encoded by SEQ ID NO:1. As described in Example 3, antiserum specific for hsOAF protein was used to detect secretion of hsOAF by breast carcinoma cell lines. The secretion levels of hsOAF protein were consistent with the different levels of msOAF mRNA expression. Highly metastatic cell lines showed much stronger hsOAF secretion than did low metastatic and non-metastatic cell lines, as shown in Figure 8B of the application (attached as Exhibit 1 for the Examiner's convenience).

The functional relationship between hsOAF expression and the characteristic cancer phenotype is described in Example 4, which discloses the use of antisense to knockout hsOAF expression. Cells of the highly metastatic cell line MDA-MB-435 were treated with antisense oligos, and a selected antisense (SEQ ID NO:4) was selected for further testing. Cells treated with this antisense oligo exhibited reduced hsOAF secretion, reduced invasiveness, and other phenotypic changes characteristic of reduction or loss in metastatic potential (Figures 10A and 10B, and Figure 12, attached as Exhibits 2 and 3).

Applicants submit further evidence of the relationship between the polynucleotides of the claims and the diagnostic use for breast cancer, in the Declaration under 37 C.F.R. § 1.132 of Christoph Reinhard, filed herewith as Exhibit 3. The Declaration discusses data obtained using tissue samples from breast cancer patients and testing these samples by immunohistochemical staining with hsOAF antibody. Strong hsOAF expression was detected in all metastatic tissue samples (26/26) and almost all primary breast tumors (44/45), whereas weak staining only was found in 8 out of 24 normal breast tissue samples.

Reconsideration and withdrawal of this rejection are respectfully requested.

7. Claims 1 and 5-11 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse on the grounds that by disclosing a polynucleotide sequence encoding the human hsOAF protein, applicants have disclosed the features of the genus of hsOAF

polynucleotides. The application therefore provides description of the hsOAF polynucleotides as claimed in claims 1 and 5-11.

In support of the rejection, the Examiner has cited case law that allegedly supports the premise that a generic statement defining a genus by functional activity fails to provide adequate written description of the genus. Applicants submit that the case law does not support the rejection, as discussed below.

The Examiner cited Fiers v. Revel, 25 U.S.P.Q 2d 1601 (Fed. Cir. 1993) for the statement that written description requires "more than a mere statement that it is part of the invention and a reference to a potential method of isolating it," (Office Action, page 7, lines 2-4). Fiers was an appeal of a decision granting priority in a three-way interference proceeding, so the focus was on earliest conception date of the complete nucleotide sequence of a DNA encoding β-IF. The Court agreed with the Board and held that conception of a DNA requires definition of the substance other than by its functional utility (25 U.S.P.Q. 2d at 1605), and concluded, "that conception of the DNA of the count did not occur upon conception of a method for obtaining it," (25 U.S.P.Q. 2d at 1605). This situation is distinguished from the present case, wherein the applicants clearly disclose the DNA sequence of the claims, as well as a definite and limited number of variants of the disclosed DNA molecule, which are defined as yielding specific conservative amino acid substitutions, or yielding SEQ ID NO:2 as disclosed.

Another case cited by the Examiner, Eli Lilly, 43 U.S.P.Q.2d 1406 (1991), is not on point. The patent application disclosed a rat sequence for insulin, and contained one constructive example of how to obtain human sequence, but provided no disclosure of which amino acids to substitute, add or delete from the rat sequence to obtain the human sequence. In contrast, the present invention does teach the substitution of one or more conservative amino acids in a disclosed sequence. The Court in Lilly stated, "Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." (43 U.S.P.Q. 2d at 1568.) That statement is not applicable to the present situation, where the material, the gene encoding the hsOAF protein, is specifically known to exist, and so a situation involving the absence of knowledge as to what that material consists of simply is not applicable to the present claims.

The Lilly case presented a situation in which the applicants claimed a nucleotide sequence from one species, wherein they disclosed a polynucleotide sequence from a different species, and the application did not suggest specific amino acid substitutions, additions or deletions in order to derive the second polynucleotide sequence from the first. The court specifically declined to apply this reasoning to a situation such as the present one. "We will not speculate in what other ways a broad genus of genetic material may be properly described, but it is clear to us, as it was to the district court, that the claimed genera of vertebrate and mammal cDNA are not described by the general language of the 525 patent's written description supported only by the specific nucleotide sequence of rat insulin." (43 U.S.P.Q. at 1569.) Thus, the Lilly case does not support a position that disclosure of a gene sequence encoding a specific protein fails to provide written description for variants of that same gene.

The Amgen case cited by the Examiner, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991), also is not on point. The Amgen case relates to reduction to practice for purposes of priority of invention, not to written description. The court held that the inventor would have to clone the sequence in order to obtain the sequence information, as the amino acid sequence was unknown. The holding of the case relates to conception, not written description, and to best mode. However, applying the reasoning to the present case, applicants' specification does not present a situation where the amino acid sequence is unknown; on the contrary, the amino acid sequence is known, and also known are possible nucleotide changes resulting in conservative amino acid sequence substitutions that can be performed to obtain other members of this genus.

The goal of the written description requirement is to prevent applicants from claiming priority to earlier applications if the current application discloses new matter not present in the earlier applications (Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Further, In re Kaslow affirms that "the test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language" (707 F.2d 1366, 1375 (Fed. Cir. 1983)). The Examiner has misapplied the written description requirement in this case.

While the current application is a continuation of an earlier application, the claimed subject matter is fully supported by the specification of the current application, and therefore the applicant does not need to demonstrate literal support in the specification for sequence variants of SEQ ID NO:1 and SEQ ID NO:3.

For the foregoing reasons, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph (written description) is respectfully requested.

All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,
Joerg Kaufmann et al.
DAVIS WRIGHT TREMAINE LLP

By _____
Jane E. R. Potter
Registration No. 33,332

2600 Century Square
1501 Fourth Avenue
Seattle, WA 98101-1688
Phone: (206) 628-7650
Facsimile: (206) 628-7699